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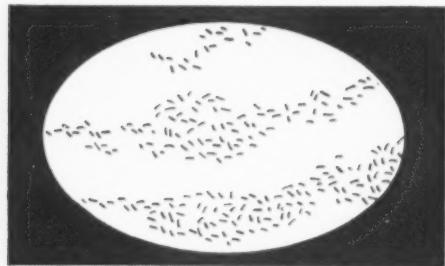
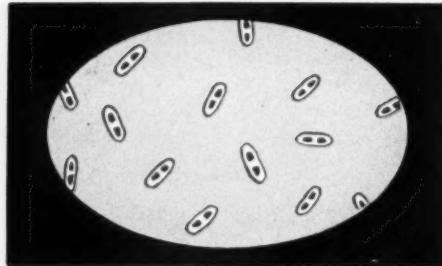
## CONTENTS

THE A. B. C. OF ANTIMICROBIAL THERAPY, <i>Harrison F. Flippin, M.D.</i> , Philadelphia, Pa. ....	55	LUETIC OSTEOMYELITIS, <i>Walter L. Bailey, M.D.</i> , Wilmington, Del. ....	71
PROBLEMS AFFECTING THE MAL-UNITED AND UN-UNITED FEMORAL SHAFT FRACTURE, <i>Paul C. Colonna, M.D.</i> , Philadelphia, Pa. ....	63	EDITORIALS ..... MISCELLANEOUS ..... BY-LAWS, MEDICAL SOCIETY OF DELAWARE ..... BOOK REVIEWS .....	73 74 74 75

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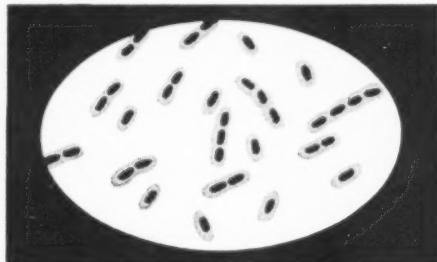
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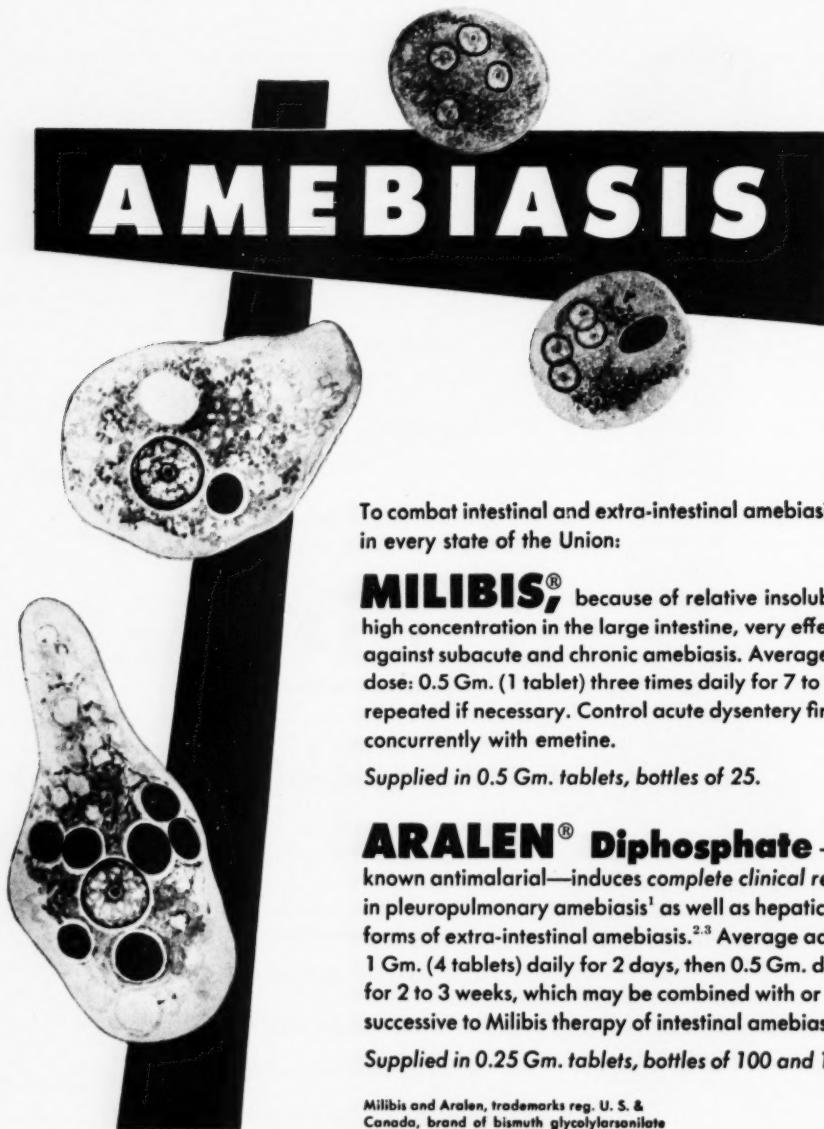
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1. Lindsay, A. E., Gossard, W. H., and Chapman, J. S. *Dis. Chest.* 20:533, Nov., 1951.
2. Conan, N. J., Jr.; *Am. Jour. Med.*, 6:309, Mar., 1949.
3. Emmett, J. *J.A.M.A.*, 141:22, Sept. 3, 1949.

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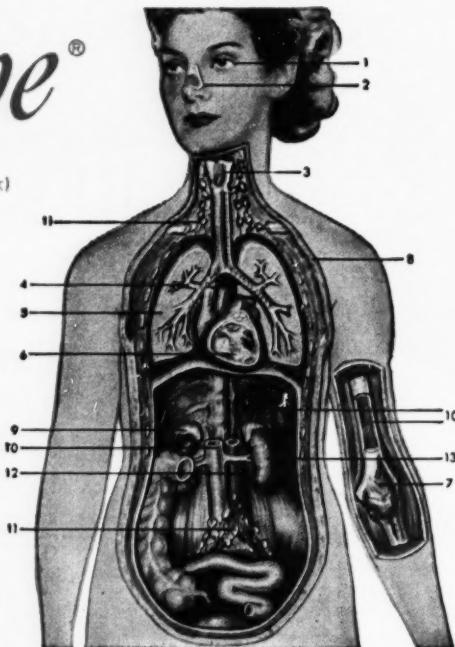


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\*Food For Your Heart, a Manual for Patient and Physician, Department of Nutrition, Harvard School of Public Health, Harvard University, The American Heart Association, Inc., New York, 1952. Copies available through local Heart Association.

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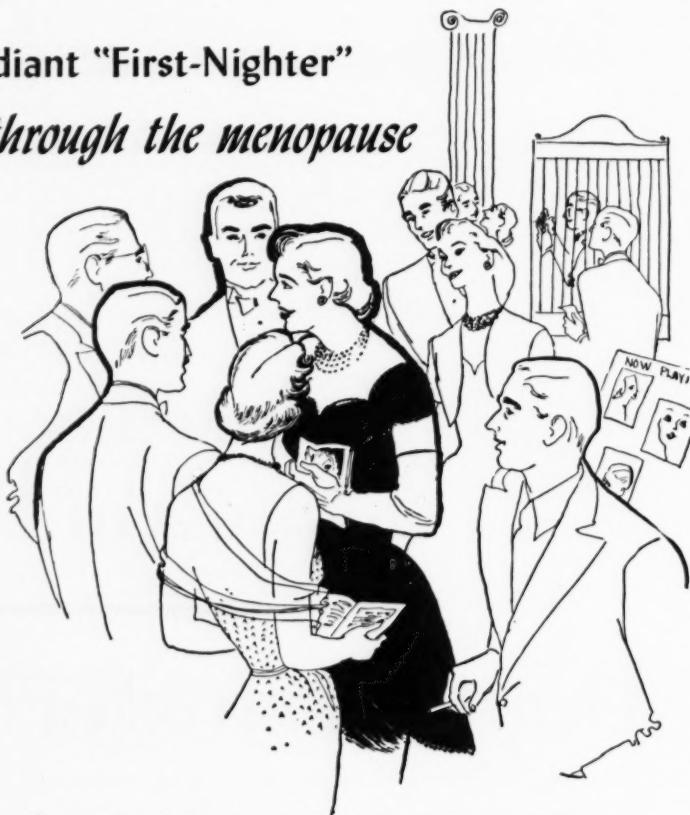


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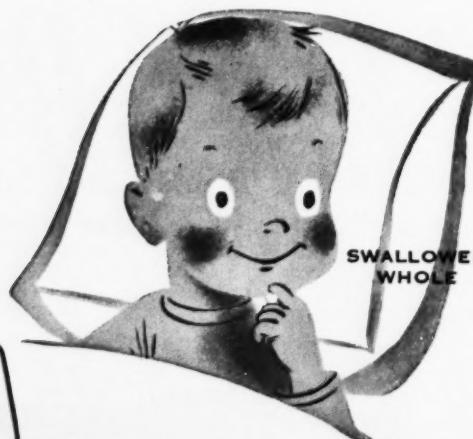


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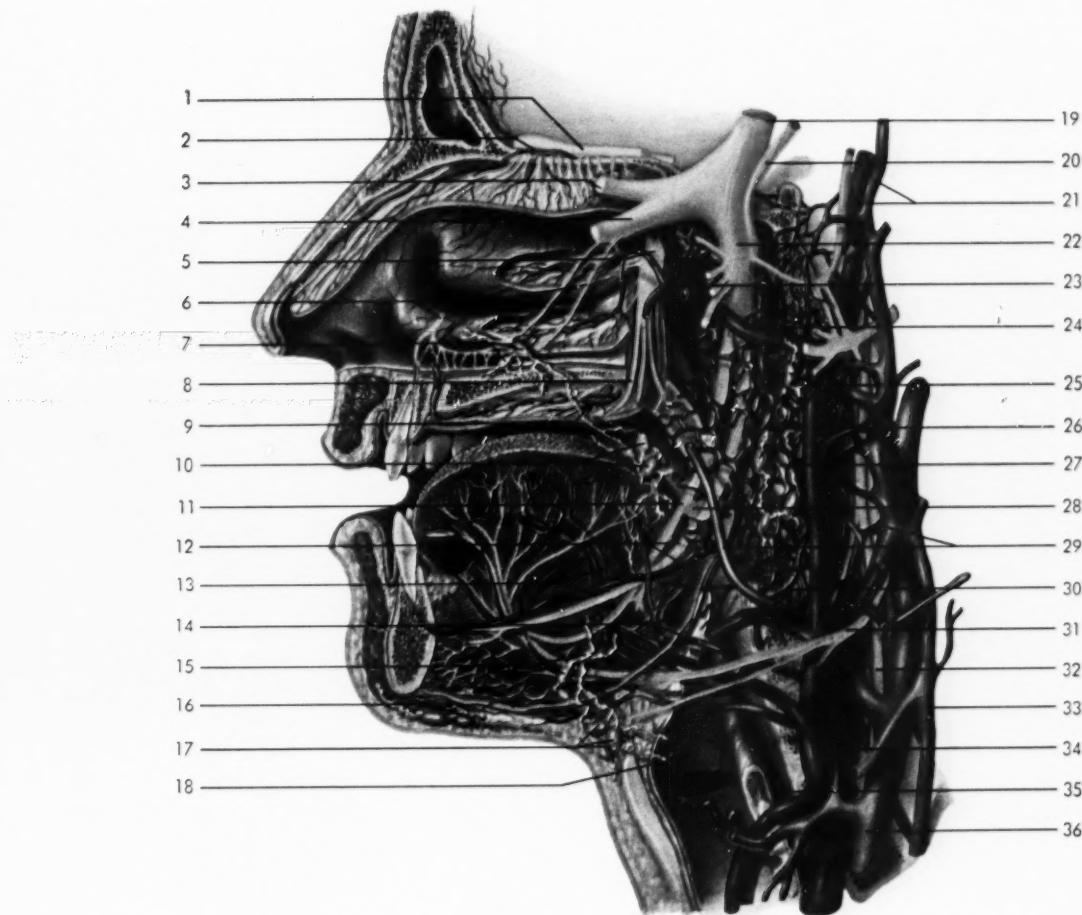
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|--|--------------------------------------|--|---------------------------------------|
| 1. Olfactory nerve                                       | 10. Buccinator lymph nodes           | 19. Sensory root of trigeminal nerve   | 28. Oropharynx                        |
| 2. Anterior ethmoidal artery                             | 11. Lingual nerve                    | 20. Motor root of trigeminal nerve     | 29. Anterior & posterior facial veins |
| 3. Ophthalmic nerve                                      | 12. Inferior alveolar nerve & artery | 21. Superficial temporal artery & vein | 30. External maxillary artery         |
| 4. Maxillary nerve                                       | 13. Lingual artery & vein            | 22. Mandibular nerve                   | 31. Hypoglossal nerve                 |
| 5. Sphenopalatine ganglion                               | 14. Mylohyoid nerve & artery         | 23. Sphenopalatine artery              | 32. Vagus nerve                       |
| 6. Anterior, middle & posterior superior alveolar nerves | 15. Supramandibular lymph nodes      | 24. Internal maxillary artery          | 33. External jugular vein             |
| 7. Maxillary lymph nodes                                 | 16. Submental lymph nodes            | 25. Parotid lymph nodes                | 34. Internal carotid artery           |
| 8. Anterior palatine nerve                               | 17. Submaxillary lymph nodes         | 26. External carotid artery            | 35. Esophagus                         |
| 9. Great palatine artery                                 | 18. Trachea                          | 27. Pterygoid venous plexus            | 36. Internal jugular vein             |

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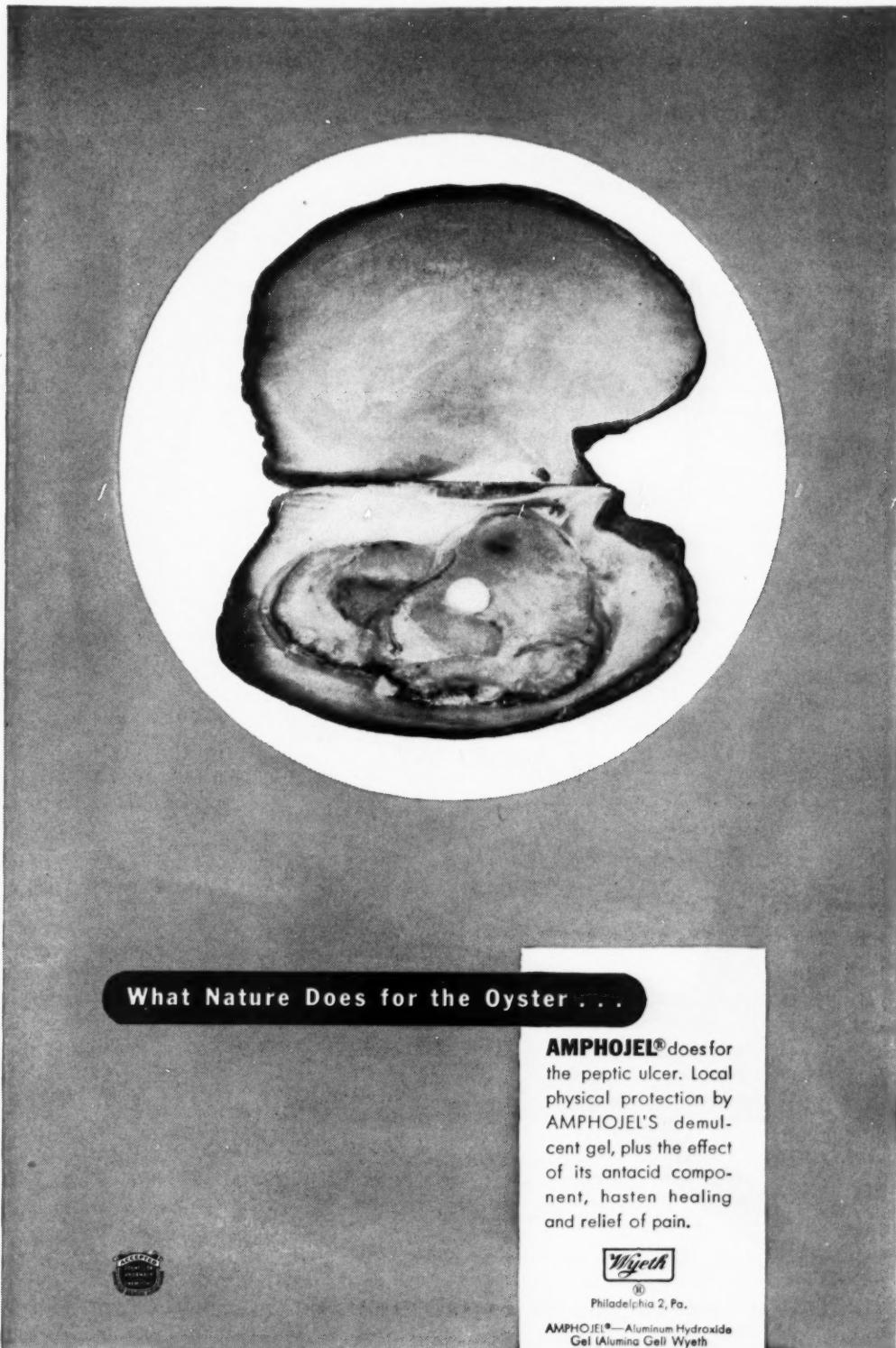
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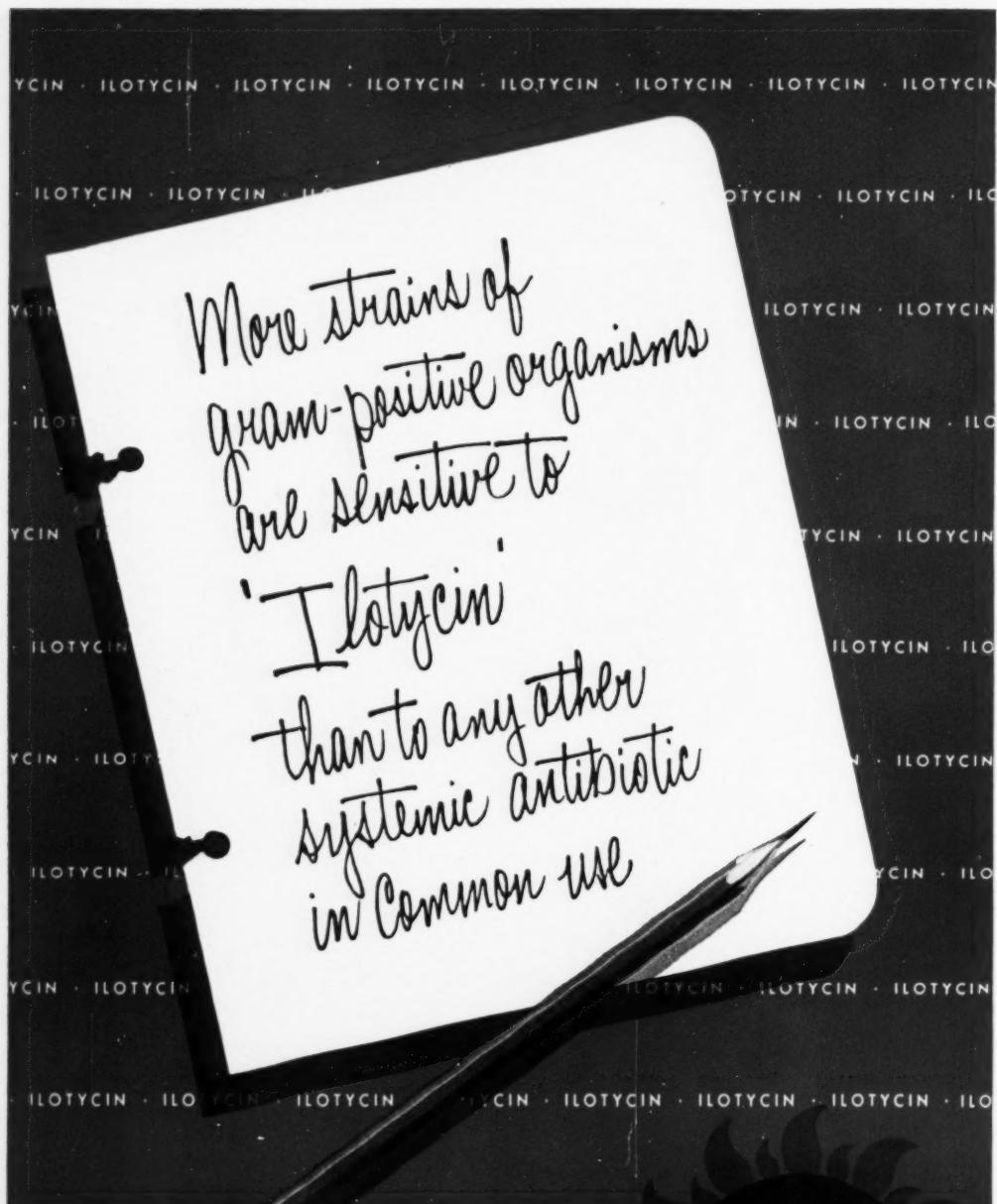
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## THE A. B. C. OF ANTIMICROBIAL THERAPY\*

HARRISON F. FLIPPIN, M. D.,\*\*  
Philadelphia, Pa.

The practice of medicine offers no greater satisfaction than the successful treatment of a patient with a severe infection which, prior to modern antimicrobial therapy, proved highly or uniformly fatal. Early and accurate diagnosis, followed by the proper use of these agents leads directly to this earned reward. Nevertheless, certain factors, such as the spectacular multiplication of available antibiotics and the increasing use of combinations of these agents, has tended dangerously to obscure those fundamental principles which are inherent to the success of this type of therapy. As a result of these factors, there seem to be increasing numbers of drug-resistant bacteria and of superinfections with endogenous bacteria and fungi which are likewise resistant to these agents, as well as an increasing incidence of untoward reactions to these drugs.

A fundamental requirement to successful treatment with any drug is that the physician have the clearest possible understanding of the therapeutic agents he prescribes. For the most part, the practicing physician is bewildered, and justly so, by the complications of antimicrobial therapy. The need is great therefore for a simple guide to the intelligent use of these drugs, although the time is not yet ripe for such an undertaking. The chief obstacle to the solution is our failure to understand fully the mode of action of these drugs and the nature of many of the toxic reactions associated with their use. These factors have impeded progress for a better understanding as to their synergistic and antagonistic activities, the development of bacterial resistance and cross-resistance, and the untoward reactions following their administration. Nevertheless, through the com-

petitive research efforts of the pharmaceutical industry in hopes of finding more effective and less toxic agents the number of these drugs steadily increases, which makes it virtually impossible for a busy practitioner to evaluate properly the available antimicrobial agents. Until these fundamental problems are more fully understood, the practicing physician can best contribute to the welfare of his patient and to the advancement of knowledge in this field by following certain principles of antimicrobial therapy in infectious diseases.

### EARLY DIAGNOSIS OF INFECTIOUS DISEASES

The length of time that elapses between the onset of the infection and the beginning of treatment is not necessarily of great importance, except in those more serious diseases, such as infections involving the blood stream, the meninges, and the endocardium. Nevertheless, one should institute therapy as soon as the clinical diagnosis has been made and the necessary material has been collected for laboratory study. In a number of cases of infectious disease it is impossible to be sure of the diagnosis when the patient is seen for the first time. Although antibiotic therapy need not be withheld until a bacterial diagnosis has been established, there are occasions when it is justifiable to wait for further developments in order to arrive at a more accurate diagnosis, or to see if the condition will not improve spontaneously. Today, however, with the widespread use of antibiotics, the physician often finds it difficult to withhold these miracle drugs at the time of his initial visit. The patient demands relief and the relatives are insistent that something be done. To succumb to these pleas is often literally a fatal mistake. These therapeutic agents may modify the disease so as to confuse the diagnosis and, as a result, we are seeing an increasing number of patients in whom the classical signs and symptoms of disease are masked or modified by these drugs. For this reason, it

\*Read before the Medical Society of Delaware, Rehoboth, September 9, 1952.

\*\*Associate Professor of Medicine, University of Pennsylvania.

is sometimes advisable to discontinue all chemotherapy in those patients in whom the response has been unsatisfactory and in whom the diagnosis is uncertain. Not only does this give the disease an opportunity to manifest itself more definitely, but also eliminates the possibility of drug toxicity.

#### ACCURATE DIAGNOSIS OF INFECTIOUS DISEASES

As a result of the effectiveness of these new therapeutic agents, there has been a definite trend towards carelessness in diagnosis both from a clinical and laboratory standpoint. Obviously, there are many infections which respond dramatically to the antibiotics without an accurate diagnosis. In a number of instances, the causative organism can be accurately recognized without laboratory aid, by virtue of the characteristic clinical picture of the disease. In certain infectious diseases, however, the diagnosis to a large extent is one of exclusion and in such cases it is often necessary to accumulate considerable clinical, laboratory, and X-ray data. It is in this group that the proper selection of laboratory tests, together with an adequate history and physical examination aid greatly in establishing an accurate diagnosis.

#### I. ETIOLOGICAL DIAGNOSIS

In view of the action of the antibiotic drugs, the determination of the causative agent is the most important single factor in the successful management of infectious diseases. Unfortunately, the wide therapeutic range of these drugs has resulted in a failure in most instances to establish an etiological diagnosis. Usually, the necessary laboratory studies are reserved for cases failing to respond to therapy. For this reason, accurate figures dealing with the treatment of large groups of infectious diseases are becoming increasingly difficult to assemble and as a consequence data regarding the use of the newer antibiotics are limited. Although these newer drugs possess a broader spectrum of activity, certain patterns have developed which demonstrate the fact that certain groups of bacteria are more easily controlled by different antibiotics. For example, certain strains of Friedlander's are more sensitive to aureomycin than to streptomycin. Many strains of staphylococci are resistant to penicillin, but will respond to aureomycin and chloramphenicol. Typhoid infec-

tions are best treated with chloramphenicol. Not infrequently, a unique situation exists wherein an antibiotic with a limited range of activity is the best drug for an infection, such as polymyxin in pseudomonas infection. In other words, successful antibiotic therapy is becoming a more specific form of treatment and depends to a certain degree on specificity of action—hence, the importance of knowing the causative agent in each infection in order to administer the most suitable antibiotic. Theoretically, this should be done routinely, but from a practical standpoint, this is difficult to carry out. Therefore, there must be some middle road between the practice of giving antibiotics indiscriminately to everyone with an elevation in temperature and that of withholding antibiotic therapy until a definite diagnosis is established. Certainly, all serious infections, such as those involving the blood stream, the meninges, the endocardium, and those infections which fail to respond satisfactorily, demand efforts on our part to establish an etiological diagnosis.

Once the organism has been isolated, antibiotic therapy can be selected intelligently for most infections without resorting to sensitivity tests, except when one is dealing with bacteria, different strains of which are known to exhibit wide variations in susceptibility to the antibiotics under consideration. It appears to be generally true that stains of gonococci, pneumococci, and group A. Hemolytic streptococci are quite uniform in their susceptibility to a given antibiotic. Other organisms, obviously, differ widely in their antibiotic sensitivity, such as staphylococci, enterococci, and proteus organisms. Although the determination of bacterial sensitivity to antibiotics is a procedure widely employed, it is one which is not infrequently misleading to the physician. The use of these tests is based on the assumption that the effectiveness of the various chemotherapeutic agents determined by in vitro tests parallels the therapeutic results of these agents. Clinical results are, of course, influenced by the degree to which the particular antibiotic is distributed in the body and it is a common experience that the therapeutic effectiveness differs from the results reported in in vitro tests. In this connection, the clinical activity of penicillin is especially

likely to be under-estimated in in vitro tests. Infections due to a strain only slightly susceptible to concentrations of penicillin employed in laboratory tests and moderately or highly susceptible to other antibiotics, may clinically respond more rapidly to penicillin because of the higher blood and tissue concentrations readily obtainable with the latter drug. In general, it is wise to consider sensitivity tests as performed in the ordinary laboratory as only qualitative guides to distinguish susceptible from non-susceptible organisms.

In order to provide more rapid information to the physicians, we are employing in our laboratory the following routine. Organisms are tested for sensitivity to penicillin, streptomycin, aureomycin, chloramphenicol, and terramycin at the concentration easily obtained by moderately intensive chemotherapy. Organisms are reported as sensitive or resistant. Any organism found resistant to any of these agents is studied by serial tube dilution for the antibiotic of choice for this organism. Because of the high sensitivity of streptococci (enterococci excluded), pneumococci, *H. influenzae*, *neisseriae* to either or both penicillin and the wide spectrum antibiotics, these organisms are not tested routinely for response to antibiotics. However, all staphylococci, enterococci, coliforms, *Shigella*, *proteus*, *Salmonellae*, and *Klebsiellae* organisms are studied. In addition, all organisms in cases of subacute bacterial endocarditis are tested to penicillin by serial tube dilution technique.

In view of the above, the physician must be familiar with the rapid progress which continues in the field of infectious diseases. New types and new distribution of etiological agents are calling for new diagnostic methods. Not only must the material for study be collected properly, but such information as the stage of the disease or duration of illness, pertinent signs and symptoms, and the type of therapy being employed should be recorded.

## II. CLINICAL DIAGNOSIS

The diagnosis of infections cannot be made merely from laboratory studies. It remains for the physician to determine the etiology, not only from these findings but from a detailed history and careful physical examination.

**A. History Taking.** One of the most important steps in arriving at a diagnosis is to recognize and note the earliest symptoms of the disease. It is for this reason that the general practitioner is in an enviable position to record such facts before starting chemotherapy, which greatly adds to the stock of common knowledge. Therefore, the importance of a thorough history cannot be over-emphasized. Not infrequently, valuable information pertaining to the patient's illness can be elicited, not only from the patient, but from other members of the family. The history of an urban inhabitant drinking raw milk in the country; the removal of ticks from a dog in the late spring or early summer; recurrent bouts of furunculosis, diarrhea; previous medications; trauma; a recent tooth extraction; contact with animals, and many other leads will often supply the needed information. Today, we are often too busy to take a detailed history before starting treatment.

**B. Physical Examination.** It has been said facetiously, but with some degree of truth, that if a patient does not improve after 48 hours of antimicrobial therapy, a physical examination should be performed. Certainly, no patient should receive any therapy without first having a thorough physical examination. It is true that not infrequently the only abnormal physical finding in a case of infectious disease is that of fever. However, this does not excuse the physician from thoroughly examining all parts of the body for possible diagnostic clues. Although the common denominator in systemic infections is fever, it does not follow that all fevers are due to infection, although in this chemotherapeutic age there is a growing tendency to treat all fevers as such until proven otherwise. If perchance the therapeutic test is unsuccessful, then one is confronted with the problem of arriving at an accurate diagnosis. It is in this so-called failure group that we meet most of our diagnostic problems today. Fortunately, however, most infections, if untreated, will sooner or later give rise to characteristic symptoms, physical findings, or abnormalities of laboratory tests which, taken singly or together, will point the way towards a more accurate diagnosis. There are probably fewer cases of fever of undetermined etiology since the ad-

vent of modern therapy because many infections are eradicated by these agents without their exact location or nature being known. As mentioned previously, recognition of most infectious diseases is not difficult, as in many instances the causative organism can be accurately recognized without bacteriological proof by virtue of the classical clinical picture resulting from the infection. Again demonstrating the importance of recognizing and recording the early signs of the disease.

#### PROPER USE OF ANTIMICROBIAL AGENTS

*Penicillin.* Penicillin, by virtue of its bactericidal action remains the most effective antibiotic against the majority of bacterial infections and, since it is least expensive and toxic, it remains the drug of choice in the treatment of most of the infectious diseases encountered in this part of the world. Certainly, very few lives will be lost by administering penicillin initially and, if subsequent clinical and laboratory studies of the disease are such as to demand it, then employing one of the other antibiotics. Penicillin continues to be the drug of choice for all gram-positive bacterial infections including pneumococci, staphylococci, and Hemolytic and Non-Hemolytic streptococci infections. In addition, it is the most effective drug for the treatment of syphilis, gonorrhea, anthrax, and actinomycosis. The confusion concerning penicillin administration is, in considerable measure, attributable to the variety of preparations available. The relative advantages of the five most commonly employed dosage forms may be summarized as follows: (It should be pointed out that the recommended frequency of dosage is dependent upon the type and severity of the infection under treatment.)

1. *Crystalline benzyl penicillin in aqueous solution* administered intramuscularly, 100,000 units. Peak plasma level: 3.0 units. Time after administration: 15-30 minutes. Total duration of therapeutic plasma level: 3 hours. Recommended interval for injections: 3 to 12 hours. Advantages: Lowest cost per dose, most rapid action, highest peak level with consequent greatest diffusion into serous cavities and abscesses, shortest duration of toxic reactions. Disadvantages: Necessity for frequent

(2 to 3 daily) injections, inconvenient at home.

2. *Procaine penicillin with sodium carboxymethyl-cellulose prepared for aqueous suspension* (Crystacillin) 300,000 units administered intramuscularly. Peak plasma level: 1.0 units. Time after administration: 2 hours. Total duration of therapeutic plasma level: 24 hours. Recommended frequency of doses: 12 to 24 hours. Advantages: Requires only a single daily injection for most infections. Most economical preparation for routine hospital use. Disadvantages: High plasma levels are not obtained even with frequently repeated doses.

3. *Procaine penicillin with aluminum monostearate in oil*, intramuscular administration, 300,000 units. Peak plasma level: 0.5 units. Time after administration: 1 hour. Total duration of therapeutic plasma level: 48 hours (in most instances 96 hours). Recommended frequency of doses: 48 hours. Advantages: Most convenient preparation for home administration. Disadvantages: Toxic and allergic reactions to penicillin, procaine or oil, although rare, are of long duration.

4. *Penicillin*, buffered, oral tablets, 200,000 units. Peak plasma level: 0.4 units. Time after administration: 30 minutes. Total duration of therapeutic plasma level: 3 hours. Recommended frequency of doses: 3 to 6 hours. Advantages: Ease of administration, especially at home. Disadvantages: Greater cost.

5. *Neo-Penil in aqueous suspension (hydroiodide of diethylaminoethyl ester of penicillin G)\** 500,000 units administered intramuscularly. Peak plasma level: 0.8 units. Time after administration: 2 hours. Total duration of therapeutic plasma level: 24 hours. Recommended frequency of doses: 12 to 24 hours. Advantages: Requires only a single daily injection for most cases. Especially recommended for chronic lung conditions. Disadvantages: High plasma levels are not obtained even with frequently repeated doses.

It may be seen that the characteristics of

\*Neo-Penil is the trademark of Smith, Kline & French Laboratories, Philadelphia, for the diethylaminoethyl ester hydroiodide of penicillin G. In the European literature this ester is variously identified as Leocillin (Leo Pharmaceutical Products, Copenhagen, Denmark); as Estopen (Glaxo Laboratories, Ltd., England); as Bronchocilline (Laboratoire Roger Bellon, France); and by certain investigators as LG1, to distinguish it from the hydrochloride, which they identify as LG2.

these preparations provide advantages for specific purposes. The use of procaine penicillin in aqueous suspension once daily is less expensive than aqueous penicillin given at three or four hour intervals, and is adequate for most infections. When such infections as meningitis or endocarditis are present, however, the low level concentrations afforded by procaine penicillin or Neo-Penil will not provide sufficient diffusion and frequent intramuscular administration of aqueous crystalline penicillin is indicated. In the home, the advantage is evident of using procaine penicillin with aluminum monostearate in oil so that injections may be given at one or two day intervals. Also, under these circumstances, oral penicillin given at three hour intervals in doses of 200,000 units for the average adult provides effective plasma levels. A recently introduced compound, benemid, offers considerable promise of increasing the usefulness of oral penicillin, as well as aqueous crystalline penicillin in such cases as subacute bacterial endocarditis due to a relatively penicillin-resistant organism. This benzoic acid derivative, given in 0.5 gm. doses four times daily, exerts the same action in enhancing penicillin blood levels as was manifested by carinamide in much larger dosage. Benemid has been incorporated into the oral penicillin preparations in such fashion that a pill containing 200,000 units of penicillin and 0.5 gm. of benemid, taken every 6 hours, will produce sustained therapeutic levels in the blood.

*Neo-Penil.* A new penicillin ester, Neo-Penil (the hydriodide of diethylaminoethyl ester of penicillin G, known generically as penethamate hydriodide), has been shown to produce higher concentrations of penicillin in certain body tissues or organs than do the commonly employed penicillin salts. The concept of penicillin derivatives having affinity for certain tissues or organs of the body is not new, but this is the first instance in which the phenomenon has been observed to a degree that is therapeutically significant. Animal and human experiments have shown that Neo-Penil has a far greater affinity for the lungs than have the other penicillin preparations. In addition, animal experiments indicate a high penicillin level in the brain fol-

lowing the administration of the antibiotic in this esterified form. Experiments in humans have demonstrated unusually high penicillin levels in the cerebro-spinal fluid following its administration. Since these unusually high tissue concentrations occur in the absence of high blood levels, it is felt that the tissue levels are due to the pharmacological property of the drug and not merely to a high blood-tissue diffusion gradient. During the past year, this new penicillin compound has been studied at the Philadelphia General Hospital and found to be highly effective in bacterial pneumonia, lung abscess and bronchitis as well as a valuable adjunct in the treatment of bronchiectasis.

*Streptomycin.* The development of aureomycin, chloramphenicol, and terramycin has to a significant degree diminished the importance of streptomycin (dihydro-streptomycin) as a therapeutic agent, except that streptomycin remains uniquely valuable for the treatment of tuberculosis and should be reserved for the same; except in those instances where it is used in conjunction with other antibiotics, or in resistant infections. Dosage schedules vary according to type and severity of infection.

*Aureomycin, Chloramphenicol, and Terramycin.* For the most part these newer chemotherapeutic agents have a similar range of antibacterial activity and are usually referred to as the wide spectrum antibiotics, namely certain virus diseases and rickettsiae, both gram-negative and gram-positive bacteria, including penicillin-resistant, streptomycin-resistant, and streptomycin dependent organisms. Which of these drugs is used is usually merely a matter of personal preference or habit, but it is important to recognize the few individual differences in behavior in this group. Best known is the strikingly greater effectiveness in typhoid fever of chloramphenicol. Dosage for these drugs ranges from 2 to 4 gms. daily in divided doses every 4 to 6 hours.

It is to be remembered that whereas penicillin and streptomycin in adequate concentrations are bacteriocidal and in lower concentrations are bacteriostatic, the action of aureomycin, chloramphenicol, and terramycin is merely bacteriostatic. As a consequence, ad-

ministration of the latter agents should be continued several days longer after defervescence than is necessary with penicillin and streptomycin.

*Polymyxin.* Although polymyxin B sulfate is an agent of considerable toxicity, its unique effectiveness in infections due to *pseudomonas aeruginosa* has justified its introduction into clinical practice. This antibiotic should be employed parenterally only in hospitalized patients, since careful observation for renal damage is essential to its safe use. Its parenteral use is justified for the serious and increasingly frequent instances of pyelonephritis, septicemia, or meningitis due to *pseudomonas*. Infections with some strains of this organism may be susceptible to streptomycin or one of the wide-spectrum antibiotics; if the infection fails to respond to these agents, a trial of polymyxin B appears justified.

*Sulfonamides.* With the introduction of the antibiotics, indications for the sulfonamides have become increasingly more restricted. Nevertheless, the sulfonamides are still indicated in the treatment of uncomplicated urinary tract infections, certain gastro-intestinal disorders, and in combination with the antibiotics in such diseases as bacterial meningitis. Because of the potential kidney irritation produced by these drugs, it seems advisable to employ triple mixtures of the sulfonamides or one of the more soluble preparations, such as gantrisin. The oral administration (an initial loading dose of 3 to 4 gm., followed by 1 gm. every 4 to 6 hours) has proved to be the most satisfactory method of administering the sulfonamides.

*Combined Antibiotic Therapy.* It is frequent practice in the treatment of infections to employ antibiotics in shot-gun fashion. This practice has been furthered by the recognition that in certain instances a definite synergistic action, or additive effect, is obtainable from certain combinations—Tuberculosis (streptomycin plus PAS); Brucellosis (streptomycin plus aureomycin); Enterococcal endocarditis (penicillin plus streptomycin); Bacterial meningitis - staphylococcal, pneumococcal, and streptococcal (penicillin plus sulfonamides); H. Influenza (streptomycin plus sulfonamides). In peritonitis and

mixed bacterial wound infections, penicillin and streptomycin have been effective, although the wider spectrum antibiotics seem equally as effective. Despite these examples, there are experimental and clinical studies which show that certain combinations result in antagonism and diminished effectiveness. Aureomycin, terramycin, and chloramphenicol have been shown to diminish the effectiveness of penicillin. The interference is apparently due to the inhibition of multiplication of organisms produced by the bacteriostatic action of the wide spectrum antibiotics; the bactericidal action of penicillin is manifested only with rapidly multiplying organisms and hence penicillin activity is impaired by the concomitant use of these bacteriostatic agents. At this time it is evident that the problem of antibiotic synergism and antagonism is far from settled. Certainly, combined therapy should be restricted to the relatively few situations in which specific combinations are of established value. For the most part, combined antibiotic therapy is useful and indicated chiefly in chronic infections. There is no justification for the use of multiple agents in most acute infections and it is certainly the part of wisdom to use single agents whenever possible.

#### PROPHYLACTIC USE OF DRUGS

These drugs are not to be used prophylactically, except when the complication to be avoided is a serious one and one which occurs frequently in the absence of precautions. Certainly, their prophylactic use is justified in streptococcal sore throat, recurrent rheumatic fever and in patients with valvular heart disease in whom oral, colonic, rectal, or transurethral operative procedures are contemplated.

#### DRUG RESISTANT INFECTIONS

The widespread and indiscriminate use of the antimicrobial agents has resulted in an increased number of drug resistant bacteria. This increased microbial resistance that follows exposure to an antibiotic not only holds for the antibiotic itself, but also the possibility of the development of cross-resistance to other antibiotics exists. Acquired resistance results from continued exposure to sub-inhibitory concentrations of these drugs. However, the increasing incidence of penicillin-resistant

staphylococcal infections is thought to be due to the gradual reduction in numbers of naturally sensitive strains, thereby giving the naturally resistant strains an opportunity to become predominant. Occasionally, superinfections with microorganisms usually regarded as nonpathogenic will occur during antibiotic therapy and prove to be insensitive to the drug used. Such infections result from the dislocation of the normal bacterial flora of the sino-respiratory and gastrointestinal tracts.

#### DRUG TOXICITY

The untoward reactions following antibiotic therapy are becoming increasingly familiar. Penicillin remains the least toxic of the now available antibiotics and, if the reactions are not too severe, treatment can usually be continued with the aid of many symptomatic and anti-allergic remedies. Obviously, the more serious reactions demand discontinuance of the drug. Many patients can tolerate penicillin even after a previous allergic reaction to the same, thus making difficult an evaluation of the so-called hypo-allergic penicillin preparations. Vertigo and deafness are the chief toxic reactions following streptomycin therapy. Fortunately, however, with the present-day dose schedule in combination with PAS employed in tuberculosis, this complication has been markedly reduced.

Aureomycin, terramycin, and chloramphenicol frequently give rise to gastrointestinal and vaginal disorders which at times may become quite severe. Chloramphenicol may cause certain fatal blood dyscrasias. However, until a better drug is developed for the treatment of typhoid fever and certain penicillin-resistant organisms, chloramphenicol will continue to have a definite place in our therapeutic armamentarium. It is felt that the gastrointestinal and vaginal lesions are the result of altered bacterial flora which give rise to a vitamin B deficiency. Hence the advisability of administering liver extract intramuscularly and vitamin B complex orally in conjunction with the use of the wide spectrum antibiotics. The use of Yogurt, acidophilus and buttermilk all are worth a trial in cases with these reactions. Obviously, when one considers the untoward reactions associated with these agents, it is essential that

the physician who undertakes to prescribe these drugs shall exercise the same caution as when he administers any other highly useful but potentially dangerous drug.

Finally, despite the proven therapeutic effectiveness of the antimicrobial agents, it is to be remembered that they are not to be used to the exclusion or neglect of other proven forms of therapy. Furthermore, although the mode of action of these agents and the nature of many of the toxic reactions associated with their use remain obscure, a great deal has been learned concerning the use of these drugs which should serve as a deterrent to their indiscriminate use, both prophylactically and therapeutically. Until these fundamental problems are more fully understood, therefore, the practicing physician can best contribute to the welfare of his patient and the advancement of knowledge in this field by following certain principles of therapy.

255 S. 17th Street.

#### DISCUSSION

**DR. WILLIAM J. HOLLOWAY** (Wilmington): We are privileged to have had as our speaker and authority on the treatment of infectious diseases with antimicrobial therapy. Dr. Flippin has covered a broad subject with the ease and certainty that comes only with familiarity. If, in practice, we could follow the axioms set before us this morning, we would find our antibiotic problems simplified and our failures minimized. The greatest obstacle to intelligent and successful management of infectious diseases is the indiscriminate administration of antimicrobial drugs before an honest attempt is made to identify the etiological agent and evaluate the need for specific therapy.

As practitioners we should again familiarize ourselves with the basic science of bacteriology and at least have a working knowledge of the characteristics of the various infectious agents. We might then recognize the tenacious sputum of a *Klebsiella* pneumonia and guide our therapy accordingly, thereby saving twenty-four hours awaiting the bacteriological report. Conversely, when the bacteriologist informs us of infection with a type-3 pneumococcus, we should anticipate a slower response to average penicillin dosage. We

need not specialize in the science of bacteriology but we must not ignore it.

\* As clinicians, we should be able to detect the site of an infection and suspect its most probable etiological agent. For example, *E. coli* is the most frequent invader of the urinary tract and the pneumococcus the most common cause of pneumonia. Therefore, in such instances, we have some guide to the proper drug even without bacteriological studies.

The laboratory is most helpful when one has access to its facilities. As stated by Dr. Flippin, bacteriological studies are necessary when treating endocarditis, meningitis, and resistant infections. Our experience would indicate that blood cultures are an important adjunct in the management of pneumonia. I say this because of the difficulties we have encountered in obtaining satisfactory sputum specimens. The importance of routine blood cultures in pneumonia has been demonstrated by the frequency of positive blood cultures in the presence of negative sputum cultures. The technique of blood culture at the Delaware Hospital undoubtedly plays a large part in this success. The procedure of obtaining blood cultures at home is almost as easy as in the hospital; and, on the second preantibiotic visit, the physician could well be equipped for the procedure.

Dr. Flippin's comprehensive review of penicillin therapy leaves little that I may add. I would like to note that our own experience (with about thirty cases of bacterial pneumonia) at the Delaware Hospital would confirm the observation of others: that detectable penicillinemia is not necessary for clinical and bacteriological cures. We gave 500,000 units of oral penicillin every eight hours for three doses followed by 100,000 units every six hours which would not produce a persistently demonstrable blood level. However, the tissue penicillin level was apparently adequate because our cure rate was high.

We have found streptomycin valuable in combination with penicillin in the treatment of chronic lung abscesses and have a number of medical cures with approximately one month of such combined therapy. In the past week we have had occasion to treat a patient with a type-3 pneumococcal pneumonia who

failed to respond to adequate penicillin dosages (i.e.,) 300,000 units intramuscularly daily for four days, followed by 1.8 million units per day for four days. The addition of 2 gms. of streptomycin per day to the higher penicillin dosage resulted in clinical improvement in 72 hours.

The overall problems of antibiotic synergism and antagonism has become more and more confusing. We have tried to follow the dieta of Jawetz, which we feel are quite sound. He classifies penicillin, streptomycin, bacitracin, and neomycin in a group as bacteriocidal agents. The broad-spectrum antibiotics— aureomycin, terramycin, and chloramphenicol in a second group as bacteriostatic agents. The combination of two or more bacteriocidal drugs can be generally expected to result in synergism. The addition of a bacteriostatic drug to a bacteriocidal drug may produce antagonism unless the organism is a resistant to the bacteriocidal agent. The combination of two bacteriostatic drugs results in additive effect, not synergistic. This additive effect could be obtained by increasing the dose of a single bacteriostatic drug.

I hope that Dr. Flippin's words this morning will give us fortitude to lengthen our periods of watchful waiting and shorten our period of indiscriminate therapy.

DR. L. C. McGEE (Wilmington): The mark of a competent teacher in medicine is found in the ability to review his experience and pick out of that experience salient features. That is No. 1. No. 2 is the ability to present it so it is understandable.

We have been fortunate, today, as in past sessions of this Society, in hearing Dr. Flippin deal with the use of antibiotics in medicine. It is unnecessary and would be courtesy at this hour to repeat much of what he has said, which is exceedingly important, and I hope when you re-read his report in THE JOURNAL that it will serve to re-emphasize what he has said to us today. I should like to pick out just two or three points for repetition at this time.

No. 1 is that we are seeing in the medical services repeated instances of disease which appears to be due to the therapy. I am reminded that the dermatologist of the past has marked his service by the one in which the

patient gets no therapy for the first week or ten days. He looks at the lesion and tries to make up his mind what is back of it. At the end of the ten-day period he calls in the house officers and students and points out his findings, and so forth.

Now, this thing is coming into the field of internal medicine with increasing frequency, at least at the Delaware Hospital, where we, too, have to discontinue everything, and watch the patient, and sometimes find that no therapy is required.

Next, I should like to emphasize the limitations of the antimicrobial test which is so popular, that is, the disk and plate method. It is not sufficient as a guide. There are too many inconsistencies, and now we have accumulated sufficient experience in the literature wherein certain bacterial types are known to be treated by certain antibiotics. But don't be misled by a disk report, when you know this "bug" should respond to a certain drug. Go ahead and use the drug judiciously and find out for yourself how the drug works in the patient. That, after all, is the important thing; not how it works in the laboratory against the particular organism.

Why is it that we must have an occasional report, such as that put out recently concerning toxicity of chloramphenicol, for its salubrious effect on the patient? We have short memories. Every few years this sort of thing happens with new or old drugs. I think it has happened often enough for those men who are mature, long before they reach the "delinquent years" in practice, and even the younger men, to come to be conscious of this and to utilize that knowledge. We know that there is no medicine what at some time in some patient has not caused a reaction. That being true, why use indiscriminately a new preparation unnecessarily as a "shot in the dark?" Or, if you must use medicine to keep the patient happy, why not pick one of the oldest and best-known drugs to protect yourself and the patient against the reaction? That means the use of a drug which has been in the pharmacopeia for years.

Early this morning you heard reference to severe peripheral neuritis in the patient with tuberculosis. That is the sort of thing we should not have repeated, in the use of

any new preparation. I wonder if the guide to proper therapy of the patient is not seen in the way a physician treats his family?

The wife of another physician listened to me with serious intentness last week and smiled afterwards, when I proposed a certain treatment. She said: "Doctor, that is most interesting, what you have said about this drug. My daughter and I don't know there is any medicine besides aspirin."

DR. FLIPPIN: As Dr. Holloway has mentioned, some drugs have a synergistic action with others. Certainly, the sulfonamides, which are primarily bacteriostatic, can be used to advantage in combination with some of the antibiotics. Not only do they possess a definite synergistic action, but they are useful in controlling the development of resistant organisms, or super-infections.

Certainly, the problem of toxicity is one of the most important factors in the use of these antimicrobial agents. In this connection, it is of interest that the older clinicians seem to be more cautious about their widespread administration than are the younger men who have not had as much experience.

### PROBLEMS AFFECTING THE MAL-UNITED AND UN-UNITED FEMORAL SHAFT FRACTURE\*

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The fundamental principles of fracture treatment have not changed over the years, but with the event of the industrial age an increasing number of accidents involving the skeletal system have been occurring and of this number the fracture of the shaft of the femur ranks near the top of the list. The recognition and application of adequate treatment for this fracture becomes of increasing importance to physicians.

We still teach that early care of the fracture, accurate anatomical reduction and adequate protection of the bones while healing is occurring, are the cardinal principles in obtaining bony union. Bony union, however, should not be the only aim. It is essential to recognize that the old definition of a fracture being "a dissolution of bony continuity" com-

\*Read before the Medical Society of Delaware, Rehoboth, September 9, 1952.

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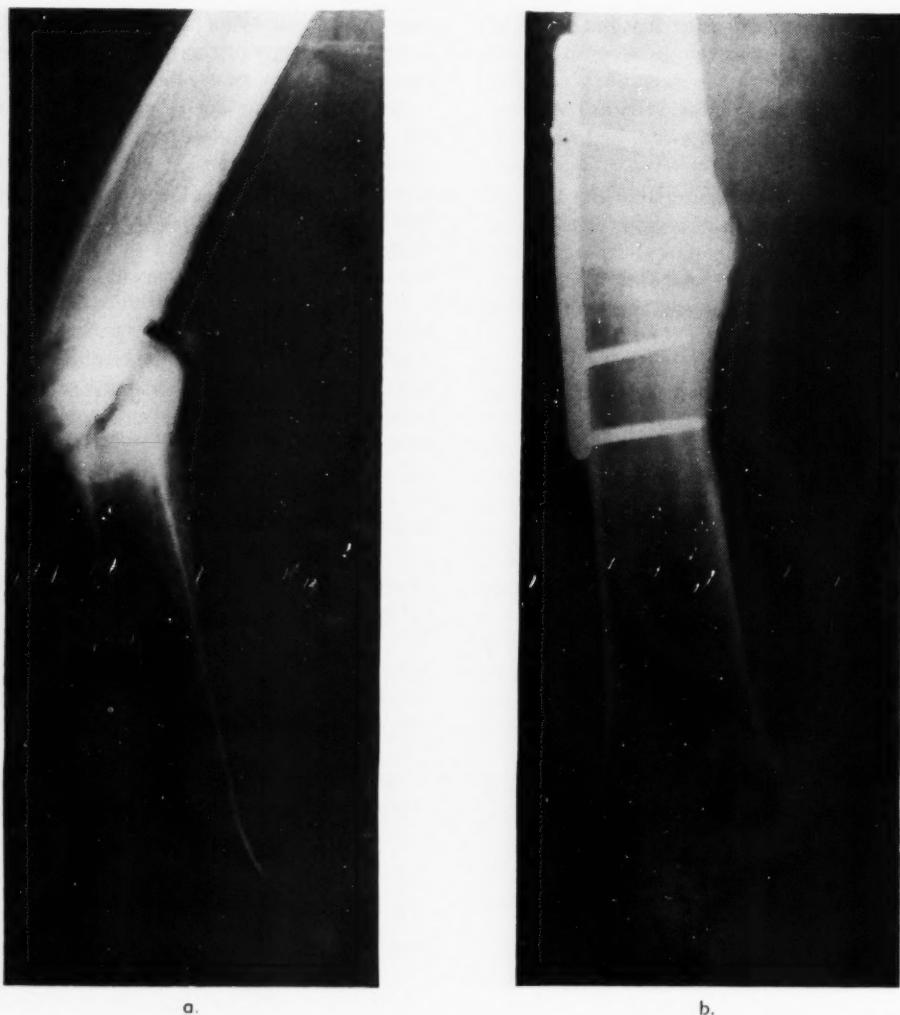


Fig. 1—Showing AP and Lat. malunited femoral fracture in (a); and after osteotomy and plate fixation in improved position (b)

pletely ignores damage affecting the soft tissues at the site of a fresh fracture. This means that the nerves, muscles, ligaments and blood vessels may and often are severely damaged and must be properly treated if we are to anticipate early functional recovery. It is the accent on early and carefully supervised rehabilitation of the patient with a fracture that means so much economically and mentally to the patient, his family, and to his employer. Therefore, it is important to stress the obvious and that is, that we can prevent many cases of mal-union and non-union by

early adequate treatment of the fresh femoral shaft fracture.

In spite of an increasing improvement in fracture treatment, we still often "leave undone those things we should have done and do those things that we should not have done."

Our remarks regarding the mal-united and un-united femoral shaft fractures will deal with a review of some of the problems we have encountered in the non-infected cases that have occurred on the Orthopaedic Service of the University of Pennsylvania during the past ten years, for they illustrate many

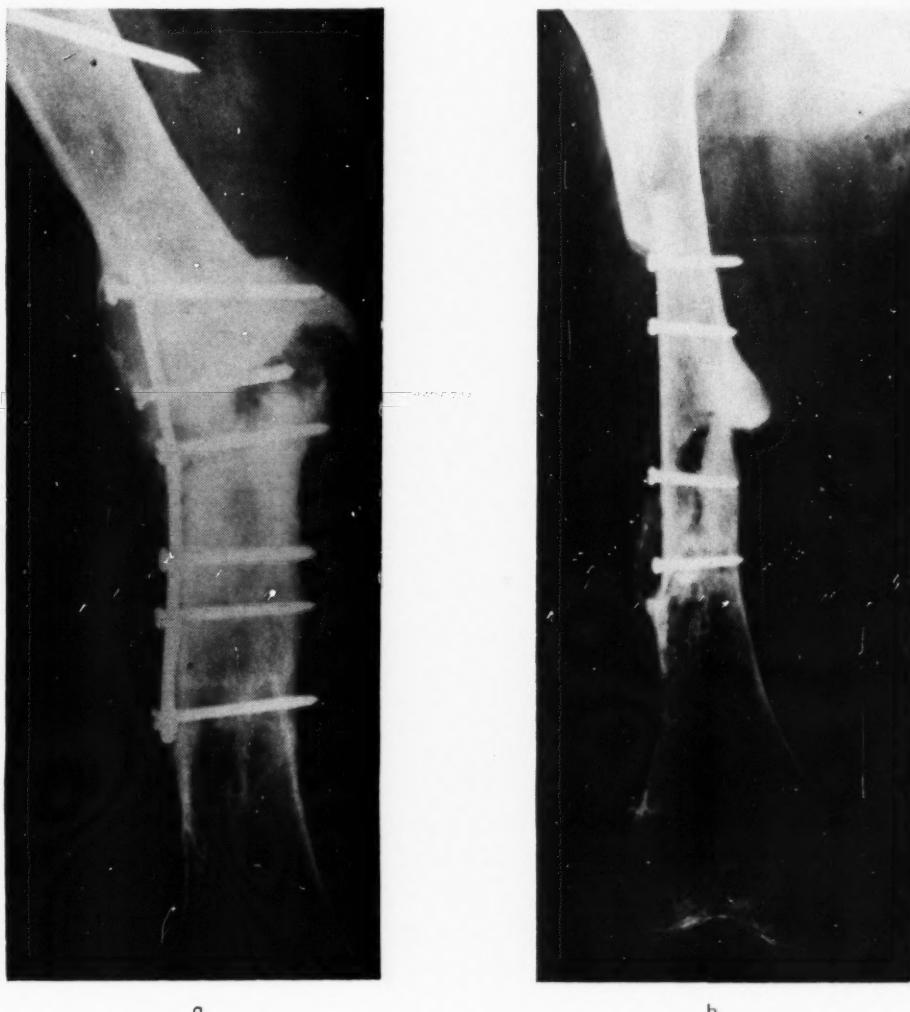


Fig. 2.—a. Showing non-union of femur following poor placing of plate and screws through the fracture site.  
b. Application of massive tibial graft with union progressing satisfactorily.

of the problems associated with this subject. The bony structure can be graphically shown by x-ray, always remembering that the soft tissue damage may be of equal or greater value in the restoration of normal function. This damage will be revealed by a careful physical examination but not by the x-ray.

#### MAL-UNITED FRACTURE

The problem of the mal-united femoral shaft fracture is, as a rule, a much simpler one to treat than is encountered when non-union is present. Many of the mild degrees of mal-union may be left untreated while in

the more severe types the mal-union may throw an added stress and strain on the ligaments about the knee and hip. For this reason, many of these require correction. A well-placed osteotomy will frequently suffice. Figure 1, a-b. Those needing correction in the upper third or middle of the femur can be well immobilized with an intramedullary nail and those in the lower third with a slotted plate—following osteotomy—until union has been re-established.

#### UN-UNITED FRACTURE

The cases with frank non-union present the



a.

b.

Fig. 3—*a*. Showing non-union of femur.  
*b*. The use of a sliding bone graft with transposition of the graft fragment and immobilization by use of plate.

greatest difficulty and many are due to technical errors in their previous treatment. Some of the more common causes of femoral shaft non-union are:

- 1) Distraction at the fracture site caused by too heavy skeletal traction or by the interposition of the surrounding soft tissues.
- 2) Too small a plate has been applied which does not give adequate immobilization to the fractured surfaces.
- 3) The insertion of screws that were too short to penetrate both cortices.
- 4) Electrolytic action that may have been

set up in the tissues when plates or screws are of different metals.

- 5) Plates breaking under excess stress and strain.
- 6) The insertion of screws through the fracture site—when the fracture is of the transverse type and the use of Parham bands encircling the bone, causing local aseptic necrosis—are practices to be condemned.
- 7) Too much hardware used.

In general, the methods employed in the care of the non-infected, un-united femoral shaft fracture should follow the basic prin-



Fig. 4—*a.* Ununited femoral fracture with pseudarthrosis.  
*b.* Following application of massive bone graft and union.

ciples enunciated by Phemister many years ago. In his conception of the healing of bone, close apposition of the fractured surfaces and rigid immobilization were of primary consideration. This, combined with the compression forces introduced by supervised weight bearing stimulates osteogenesis. The compression factor has been recently stressed by Charnley.

Whatever the method of open operation chosen for the individual problem, we feel that union can be hastened and the patient returned earlier to his job as a wage-earner if one employs the use of cancellous bone packed about the site of the old fracture. The

cancellous bone we prefer is that from the anterior portion at the crest of the ilium using autogenous rather than heterogeneous bone. Bone bank bone has been used but it is not considered as satisfactory as autogenous bone. Even when cortical bone such as the tibia is necessary for rigidity, we prefer to augment this by the use of cancellous bone packed in and about the site of non-union.

The methods we have employed in the non-union cases have been:

- (1) The use of a 4 to 8-hole vitallium or stainless steel plate fixed with screws of a

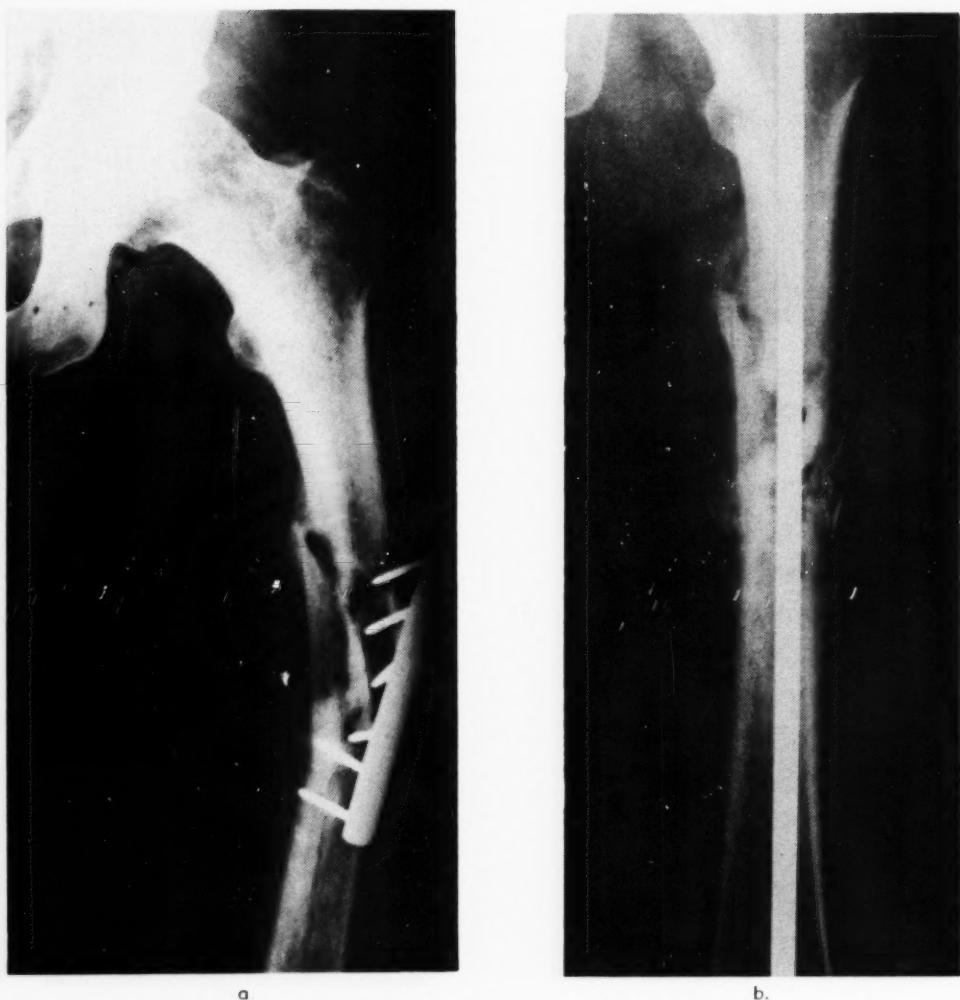


Fig. 5—*a.* Ununited fracture femoral shaft with malposition following plate fixation.  
*b.* Kuntscher rod in place with cancellous bone chips packed about site of fracture and united femoral shaft.

similar type. These penetrating both cortices at right angles to their longitudinal axis.

(2) The use of the massive bone graft, or dual graft, either laid directly on the freshened cortex or dove-tailed into slots made in the cortex assuring rigid immobilization. (Fig. 2 a-b.) We do not feel that complete removal of all the scar tissue between the bone ends is essential to union provided the bone ends have not undergone sclerosis. (Fig. 3 a-b and Fig. 4 a-b.)

(3) The use of the intra-medullary nail of Kuntscher has been reserved only for the

fractures occurring in the upper or middle third of the femoral shaft. This type of fixation in carefully selected cases is felt to be ideal for the above sites, for weight bearing provides an intermittent compression force and produces close apposition at the site of the fracture. (Fig. 5.)

#### SOFT TISSUE DAMAGE

The degree of soft tissue damage must be estimated at the time of the first examination and appropriate measures planned.

One bugbear to all operative procedures is the formation of fibrosis in the subcutaneous

tissues. This is particularly prone to occur when needless stripping of the periosteum and undue roughness of the soft tissues are employed either in the care of the fresh fracture or when further operations become necessary.

These technical errors give rise to fibrosis in the overlying muscle envelope, particularly the quadriceps, as well as causing an unnecessarily large callus formation, all of which become problems in the restoration of function in the knee joint.

A stiff knee and hip can occur from the causes mentioned above or can occur, to a modified degree, in those cases which have remained in plaster for a long period. Immobilization alone will never give rise to bony fixation of the adjacent joint but can be the cause of a troublesome stiffness and result in a prolonged convalescence while function is being restored. For this reason, as well as others mentioned, the intramedullary nail of Kuntscher has seemed an ideal method of treatment whenever the non-union occurs in the upper or middle third of the bone.

#### KUNTSCHER NAILING

The Kuntscher nailing technique is not without its individual problems and many bizarre complications have been reported. In general, the author prefers to do an open operation at the site of the non-union and after removing the pseudarthrosis if present, insert a guide wire in a retrograde manner into the medullary cavity of the proximal fragment and which exists just under the skin in the gluteal region. Then, after a nick in the skin, a clover-leaf Kuntscher nail, of adequate length and adequate diameter, is driven along the guide wire to the site of fracture. The fragments are placed in anatomical position and the nail then driven down into the distal fragment as far as the condyles of the femur. This assures exact alignment and if firmly imbedded into the condylar region, prevents longitudinal rotation of the bone. No plaster is post-operatively necessary and the patient can, after the first few weeks, begin moving the hip and knee and by the end of the 4th week be up on crutches with some weight bearing. It is again stressed that pre-operatively an estimation of the length of nail needed as well as its diameter is most

essential for success. Occasionally the medullary cavity may need to be reamed out a few inches below and above the fracture in order to have the nail set accurately and securely. (Fig. 6 a-b.) Another small but important point in the technique is to manually impact the femur at the point of non-union by pounding on the patient's heel and visually confirming the fact that the bones are in close opposition before the thigh wound is closed. If the nail is of the proper length, it will only project about one-half inch above the upper portion of the femoral shaft and will be well placed about one-half inch from the femoral articular surface at the knee joint.

This brief review stressing some of the problems of femoral shaft fractures should not close without an acknowledgement of the great boon that the antibiotics have been to the surgeon. He operates today with great confidence that aseptic precautions have been carefully observed by his assistants and himself and that the area of operation has been properly prepared. All this today is routine and careful surgery is presupposed. But in bone surgery especially, infection delays definitive treatment tremendously and while we do not advocate the employment of chemotherapy and the antibiotics routinely in clean surgery, its availability in these cases requiring major bone surgery gives additional security to the patient and to the surgeon.

#### SUMMARY

- 1) The principles underlying the treatment of fresh femoral shaft fractures have been stressed in order to minimize the development of mal-union and non-union.
- 2) Some of the frequent causes of non-union of the femoral shaft have been enumerated.
- 3) Methods which have proven satisfactory in the treatment of mal-unions and non-unions are briefly mentioned and illustrated by roentgenograms.
- 4) The indications and technical difficulties involved in the use of the Kuntscher nail have been reviewed briefly.

#### 34th and Spruce Streets

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## DISCUSSION

**DR. I. M. FLINN** (Wilmington): Whenever Dr. Colonna delivers a paper there is little left to be said. He is quite thorough, quite conservative, and extremely modest.

In the femur nature literally thirsts for union. Only when bony contact is incomplete or interrupted is there difficulty in obtaining it.

Dr. Colonna has mentioned soft tissue damage. Frequently, I must say, the soft tissue damage is increased by ill-chosen incisions. Whenever possible one should stay away from the quadriceps mechanism. Incisions along the lower aspects of the thigh in the lateral gutter are probably the best. Frequently it becomes necessary after a fracture is united to perform another operation in order to release the quadriceps mechanism.

There are plenty of dangers involved in the use of the intramedullary nail. At a recent symposium the conclusion was that some 35% of the cases have some sort of complication as a result, so that use of the nail is something that is not to be considered lightly. We, ourselves, have done four of five of these operations.

The first case we did I feel we should not have used it: it was a case of probably poor judgment. When we operated we found no infection, but the tissues didn't look just right. We inserted the nail—and two years later the leg had to be amputated. We have had only 25% complications so far.

**DR. D. J. KING** (Wilmington): If I may be permitted to have a couple of minutes. I would like to show a case that demonstrates many of the points Dr. Colonna has mentioned. If I may have the first slide, please.

Slide: This is a case of a white, thirty-four year-old male who suffered many injuries when a tree fell upon him. Amongst these injuries was a fractured femur. This occurred in May, 1951. A couple of days later the surgeon elected to do an open reduction.

You can see here that the fractured site covered by the plate—this doesn't demonstrate it too well—but screw No. 2 is interposed between the fractured ends. It is not well demonstrated here. And the screws engage one cortex—and this picture presented itself shortly after the operation. For that

reason the surgeon removed the plate and replated it. However, osteolytic changes were evident and the fracture was not maintained.

On February, 1952, nine months later, he was referred as a case of non-union.

Slide: At which time the hardware was removed and an open reduction was performed. Before going on, I might add that he had a stiff knee with just a trace of motion. The quadriceps muscles were fibrosed, and after the operation a light manipulation of his knee was performed.

Slide: In June of '52, almost four months later, the patient had been up walking around with crutches in a limited manner when suddenly he developed pain. He thought he was getting a swelling. We immediately had him brought to the hospital—and, unfortunately, this slide doesn't show the state of affairs.

Slide: But the nail had migrated, over a very short period of time. As a matter of fact, it was hours. And here, instead of it ending a half inch above here, we now find it is five and a half inches up here. This was reinserted and a few days later the man was back, walking around, and we hope that he will develop union. Perhaps one mistake in judgment was the fact that I didn't add the iliae bone, and I feel if I had, perhaps we would have had union sooner. I don't believe that union is complete.

**DR. W. L. BAILEY** (Wilmington): I don't want to discuss that paper; it is too good, but I want to ask his procedure when he has two fractures—as to the length of the nail—or how he handles that situation.

**DR. COLONNA:** Before I take up Dr. Bailey's "Sixty-four Dollar Question," I might tell you it wasn't very difficult to come down because Dr. King met me at the train and brought me all the way. I had a good lunch, so I don't think I deserve a thing except congratulations at being invited here.

The interesting case he has just shown I think is developing non-union, all right, but I think it is interesting to surmise why the pin should have gravitated or backtracked, as it were. That is most unusual. Whether it is because it was not firmly imbedded in cancellous bone just above the knee joint or whether the factors of walking and use of it in some way may have loosened it, I am sure

I don't know. I have not seen that exact complication to such a degree.

In Hugh Smith's excellent and comprehensive review of a large number with femoral fractures treated by the rod, he tells an amusing story of one man who had a Kuntscher nailing. The nail slipped down through the greater trochanter region into the femoral medullary cavity, so that when the man stood up there would be a "plunk" and when he raised his leg there would be another "plink," as the rod slipped back up into the medullary cavity.

No two cases are exactly alike, but I do think with selected cases, selected sites, familiarity with ordinary bone and joint technique, the Kunschner nail is a decided advance over the previous methods that we have had for the treatment of most fresh mal-union and non-union upper 1/3 femoral shaft fractures.

The complication of the stiff knee due to the quadriceps fibrosis is a very hard one to solve, and my own experience in releasing the quadriceps muscle from the adherent fibrosis has not been good. I have been very discouraged about the various plastic operations on the knee and various methods of getting mobility in a knee that is stiff through fibrosis of the quadriceps.

Now, the question that Dr. Bailey poses regarding the method in treating two fractures of the femoral shaft: If he is meaning the fresh fracture in the upper third, I still think they should be treated by a rod, and I think you would have to estimate to some degree—but I don't believe it would be too difficult to estimate—the length of the femur by taking seancograms. If you are dealing with a non-union, where you may have to sacrifice some bone because of the underlying sclerosis or scarring of the bone, that is a little more difficult, and one might have to cut off a protruding nail with a hacksaw to obtain the proper length of nail.

There is a nail on the market now, which I have never used, which can be added to or subtracted from. One of the surgical houses has put it out and you can screw in another length to it.

Thank you, very much, for your invitation and kind reception.

## LUETIC OSTEOMYELITIS

### A CASE REPORT

WALTER L. BAILEY, M. D.,\*

Wilmington, Del.

A. W., No. 183390, Delaware Hospital. Admission 8-4-51. Discharged 8-20-51. Admitted with three weeks' old complaint of pain and swelling left lower leg and foot. Pain kept patient awake at night. Past medical and surgical history was negative. Denied venereal disease. Occupation, truck-driver.

*Physical Examination.* Swelling left lower leg and foot, no increase in local temperature. Markedly tender along crest of tibia, lower half.

*X-ray Examination.* (Fig. 1) Destructive lesion lower half of tibia with marked periosteal proliferation.

*Laboratory Examination.* 8-6-51. Hgb. 92 per cent, 14.4 gms; W.B.C. 6700, polys 62, poly non-seg. 1, lymphocytes 32, monocytes 4, eosinophiles 1. Phosph. 4.3; calcium 11.6; Alk. phosphatase 1.0. Urinalysis, negative. Bld. serology: 8-6-51—Kolmer-Wassermann 4-plus; Kahn Standard 4-plus; Mazzini 3-plus.

*Hospital Course.* Lesion biopsied. No purulent material encountered. The periosteum markedly thickened and stripped with difficulty. Cortical bone softened and medullary canal filled with grayish white material of firm consistency.

*Pathological Report.* Osteomyelitis, non-specific, compatible with luetic osteomyelitis. Culture of wound negative. Patient received total of 6,000,000 units of penicillin during hospital stay, from which he developed a marked urticarial reaction. Incision healed per primum. Repeat Wassermann 8-17-51 was 4-plus.

*Further Course.* Referred to Dr. John H. Stokes, Syphilologist, University of Pennsylvania, for more complete work-up and suggestion as to treatment of persistent positive serology. Cardio-vascular system found to be negative, skull negative for osseous changes, but serological study of spinal fluid indicated probable meningo-vascular syphilis. Because of former reaction to penicillin, use of hypoallergenic penicillin, together with antihista-

\*Associate in Orthopedics, Delaware Hospital.

minies, suggested by Dr. Stokes. X-rays four months' postoperative are shown in Fig. 2.



Fig. 1



Fig. 2

#### BRIEF DISCUSSION

Luetic osteomyelitis is more often acquired than congenital and occurs in 0.5 to 0.7 per cent of all cases of acquired syphilis. Bones affected in order of their frequency are tibia, clavicle, skull, fibula, femur, humerus, ribs, ulna, and scapula.<sup>2</sup>

Diagnosis of this condition is not easy. Clinical symptoms are generally referable to the part involved. Roentgenographic findings are confusing and take many forms: osteitis, periostitis, osteoperiostitis, osteomyelitis, gummatous formation, forms of arthritis, and arthropathies.<sup>2</sup>

For the above reason one must consider or eliminate pyogenic osteomyelitis, tuberculous osteomyelitis, fungus infection, primary sar-

coma, and metastatic malignancy.<sup>3</sup> The early lesions can closely resemble multiple myeloma.<sup>5</sup> Final diagnosis rests on adequate biopsy and free use of laboratory facilities.<sup>2</sup>

Treatment of luetic osteomyelitis, once diagnosis is established, is preferably by penicillin. In the past bismuth muscularly yielded excellent results.<sup>1, 6</sup> Syphilis is a systemic disease, osseous involvement being only a local manifestation. Definitive treatment, therefore, should be under the direction of a competent syphilitologist.

Note—The author wishes to express his appreciation to Dr. John H. Stokes for his valuable assistance in this case.

501 Delaware Avenue.

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#### American College of Allergists

The annual conclave of The American College of Allergists will be held this year at the Conrad Hilton Hotel in Chicago April 24 to April 29.

The first four days will be devoted to instruction under the tutelage of recognized authorities and the last three to a discussion and reporting of recent advances in the field of allergy by the investigators themselves. For detailed information write The American College of Allergists, La Salle Medical Building, Minneapolis 2, Minnesota.

#### Postgraduate Institute

April 28—May 1, 1953, Bellevue-Stratford Hotel, Philadelphia. Conducted by The Philadelphia County Medical Society. Technical Exhibits. Thomas M. Durant, M.D., Director. Direct all Inquiries to 301 South 21st Street, Philadelphia 3, Penna. Registration Fee Ten Dollars. (Non-Members of Society.) A Detailed Program Will Be Mailed Out in the Near Future. We Hope You Will Be Present.

+ Editorials +

## DELAWARE STATE MEDICAL JOURNAL

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No. 3

### MARCH IS RED CROSS MONTH

Every month in the year thousands of people in need or distress reach out to the Red Cross for the help they must have, help that comes from the generous efforts and support of housewives, businessmen, industrial workers, school children, professional workers — your nextdoor neighbors — and countless others who serve their fellow man through the Red Cross.

In a time of tension and cynicism it is well to be reminded of the inherent goodness of people, to call attention to their constant voluntary efforts to make life a little better for the men and women in the armed forces, for hospitalized veterans, for disaster sufferers, and for those in need in other lands.

Although the heart and hands of the Red Cross are provided by hundreds of thousands of volunteers, money is also needed to collect blood; to provide financial assistance for servicemen, veterans, and their dependents; to

furnish emergency aid and rehabilitation to disaster victims—services that can be provided only through the voluntary financial support of millions of Americans.

Every March Red Cross volunteers turn to their neighbors and ask help in answering the call of those in need. Let us respond generously to this appeal so that we can answer the call of humanity through our Red Cross.

### WHERE DOES THE MONEY GO?

A sheet of 1953 Easter Seals came to us in the mail last week.

We've been contributing to this annual drive to "help crippled children" for several years, but when the '53 Seals came we began to think. Just where did our money go?

Inquiry brought us a good bit of interesting information. Here's something of what we learned:

This year marks the 20th year that Easter Seals have been reaching the public, seat by the National Society for Crippled Children and Adults and its affiliated societies nationwide in an effort to help the handicapped. The organization is made up of 2,000 chapters located in every state, and the District of Columbia, Alaska, Hawaii, and Puerto Rico. Easter Seals are mailed to us by the Delaware Society for Crippled Children and Adults whose office is located at 1002 Washington Street, Wilmington, Delaware.

Most of the funds we contribute — 91.7% of the total amount — remain right here in Delaware, financing services of all kinds for the crippled children and adults in our midst. Last year the organization directly helped more than 287 of these persons through its year-round program of case-finding, direct services, education, and recreation. It seeks out crippled persons who need care not given by other agencies, public or private. Any one of us can refer a crippled child or adult to the Easter Seal Society for help.

Nationally, we learned Easter Seals finance education of the public, of parents of crippled, and of professional workers for furthering acceptance and rehabilitation of the handicapped. They also support research into the

causes of crippling conditions, and direct services for aiding the development of individual state programs.

With this information, we concluded that it is important, from both the economical and the humanitarian standpoint, to help the handicapped become independent, happy and useful citizens who can earn their own way. We slipped our contribution to Easter Seals in the return envelope — more this year to meet rising costs. We hope you'll do the same! Easter — April 5th — is almost here.

#### CORRECTION DUE

The letter-head of the New Castle County Medical Society, which goes to eighty per cent of the Medical Society of Delaware, contains an omission which should be noted. At the top of the personnel column, under "Board of Directors", appear only three names. The By-Laws of the NCCMS (Page 24, Section 8, Directors) plainly state: "The Board of Directors shall consist of three members, one of whom shall be elected each year to serve for three years, *plus the President, President-Elect, Secretary, and Treasurer, Ex officio.*" (*The italics are ours.*)

When this Board of Directors meets there should be present seven members—not a mere three.

#### MISCELLANEOUS

##### Illinois Doctors Contribute

A \$59,570 contribution to help alleviate the financial difficulties of the nation's medical schools has been received by the American Medical Foundation, it was announced recently by Hiram W. Jones, Chicago, executive secretary of the foundation.

The donation, made by 2,966 Illinois physicians through the Illinois State Medical Society, included a \$400 contribution by the 20 members of the Effingham County Medical Society and an additional \$250 from the society itself. A tragic fire at St. Anthony's Hospital in Effingham, early in 1949, killed several persons.

Mr. Jones pointed out that already this year the foundation has received more than 3,600 contributions, totaling more than \$594,000, adding:

"Our 1953 goal is \$2,000,000. This is proof-positive that the medical profession has found

a solution to the serious financial problems that beset the nation's medical schools."

The foundation has raised \$2,246,401 since it began operation in 1951 to stimulate voluntary contributions from members of the medical profession for support of medical schools. In conjunction with the National Fund for Medical Education, the A.M.E.F. has distributed grants totaling \$2,819,901 to the country's 79 approved medical schools for their unrestricted use.

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#### BY-LAWS

##### MEDICAL SOCIETY of DELAWARE

###### Amendments Adopted

The following Amendments to the By-Laws of the Medical Society of Delaware were adopted by the House of Delegates on October 8, 1951. Each member should make these notations in his copy of the By-Laws, or paste this clipping therein.

###### ITEM I

Page 10, Line 6 and Line 16, Article 3, Section 6 — Dues and Assessments. Change "April 1" to "April 30".

###### ITEM II

Page 18, Line 19, Section 9 — Transfers. Change "one year" to "six months". Section 10 Bottom Line—Transfer Cards. Change "Twelve months" to "six months".

###### ITEM III

Page 10, New Amendment to Article 3, Section 6 — Dues and Assessments. Active members of this Society shall be excused from payment of annual dues and special assessments of this Society as long as they are on active duty with the Armed Forces of the United States. Said members shall pay the dues for the year in which they are inducted into service, but shall not pay the dues for the year in which they are mustered out.

###### ITEM IV

Page 10, New Amendment to Article 3, Section 6 — Dues and Assessments. Active members of this Society who retire from practice before the age of seventy and who derive no part of their income from the practice of medicine shall be excused from the payment of annual dues or special assessments of this Society, provided they are similarly excused from the payment of dues and assessments of their component county society. (Adopted September 8, 1952.)

**BOOK REVIEWS**

Side Effects of Drugs. By L. Meyler. Translated by P. H. Vuijsje and W. Mulhall Corbet. Pp. 268. Cloth, Price, \$5.50. New York: Elsevier Publishing Company, 1952.

This book has a good stated reason for being written—"Diagnoses first, Treatment afterward," but the author has destroyed the usefulness of the subject by overemphasizing the dangerous symptoms of overdosage. As the author warns, the physician must show extreme care in prescribing any drug, new or old. He outlines all of the untoward symptoms, signs, and sequelae that may occur without giving the dosage which has caused the toxic side effects and without suggesting the safe dosage or what precautions should be taken to avoid such reactions.

The information given with each drug is apparently authentic, but anyone reading of all the damaging effects of such generally used drugs as aspirin, penicillin, insulin, curare, and ACTH will never venture to use them on the basis of information presented here.

Most of the drugs, antibiotics, hormones, and vitamins listed are used daily by the busy practitioner and it is up to him to know the safe dose range before toxic symptoms develop. This information is readily available in any standard book in pharmacology.

A long list of references, mostly European, is given at the end of each chapter but the author and title are not given, only the journal and pages in which they appeared.

We fail to see the usefulness of this book in its present form.

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Pharmacology In Clinical Practice. By Harry Beckman, M.D., Director, Department of Pharmacology, Marquette University. Pp. 839, with 152 figures. Cloth. Price, \$12.50. Philadelphia: W. B. Saunders Company, 1952.

Dr. Beckman's book is unique in that it is not merely a textbook of technical pharmacology but also a book of clinical value because the drugs are arranged according to their therapeutic effects. For example, drugs are classified under Allergy, Anesthesiology, Cardiology, Dentistry, Dermatology, Endocrinology, etc. The clinical effects, nature of action, absorption and excretion, method of

administration, toxicity, and other valuable information based on the author's vast teaching experience are clearly outlined. The discussion of each subject is brief and clear.

The contents are divided into two sections. Section I, Clinical Use of Drugs, covers 714 pages. Here the pharmacologic aspects of all drugs used in daily problems which arise in medicine and dentistry are discussed. Section II supplies a few chemical and physical facts about the drugs discussed in Section I and lists some representative commercial preparations of each so that the reader would know the forms in which they are available.

This is an excellent book and is highly recommended for the physician and dentist who prescribes. It will also be found indispensable by the medical, dental, and pharmacology students who must be kept constantly informed of the uses of the numerous drugs and antibiotics.

A complete index and cross-index adds to the rapid accessibility of the information. Suggested excursions into the literature are listed at the end of each part.

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Sex After Forty. By S. A. Lewin, M.D. and John Gilmore, Ph. D. Pp. 200, Cloth. Price, \$3.50. New York: Medical Research Press, 1952.

This interesting book discusses in general terms the sex physiology of the male and female as it refers to those over forty years of age. The seventeen chapters emphasize the proper hygiene and attitudes toward married life and attempt to minimize the fears and worries one associates with the menopause and the male climacteric.

Actual case histories show how patients are rehabilitated through the proper medical supervision and at times by means of endocrine and hormone therapy.

The text includes an Atlas of Male and Female Pelvic Anatomy, in color, and about 100 drawings, photographs, and photomicrographs.

This book is written in easily understood language and is highly recommended for teachers, social workers, and lay persons who are near or over forty years of age. The book contains a glossary of medical terminology which will be found very helpful by the lay reader.

**Surgical Practice of the Lahey Clinic.** By members of the staff of Lahey Clinic, Boston. Pp. 1014, with 784 illustrations on 509 figures. Cloth. Price, \$15.00. Philadelphia: W. B. Saunders Company, 1951.

This new volume from the Lahey Clinic, coming just ten years after the first volume, presents procedures which by repetition have become standardized in that clinic. Only one procedure is presented for each type of case. The book is devoted mainly to operating technique, but includes also diagnosis, preoperative and postoperative care, choice of anesthesia, and an evaluation of end-results.

Perhaps the outstanding chapter is the one by Dr. Lahey himself on Technic of Subtotal Thyroidectomy, which covers 28,000 cases. It would be well for every neophyte in goitre surgery to read this chapter.

The chapter subjects are: thyroid gland and neck; esophagus, lungs, and heart; stomach and duodenum; small intestine; sigmoid and rectum; biliary tract; spleen, adrenal gland, and pancreas; breast; pelvis; bones and joints; brain, spinal cord, and nerves; anesthesia; and miscellaneous.

The illustrations are excellent and the index is complete.

Every experienced surgeon needs this volume to complete his modern library; the inexperienced surgeon can read it with profit to himself and to his patient.

---

**The Literature On Streptomycin—1944-1952.** By Selman A. Waksman. Cloth. Pp. 553. Price, \$5.00. New Brunswick, New Jersey. Rutgers University Press, 1952.

This is a complete reference list of actinomycetes, antagonistic properties, streptothrin and streptomycin. 5550 streptomycin publications are covered up to 1952. The author index includes cross references to all the authors of a given paper.

In view of the rapidly accumulating literature on streptomycin, annual supplements, rather than new editions of this volume, are planned. In addition, digests dealing with various uses of streptomycin will be published from time to time.

Investigators who are interested in streptomycin will find this book a useful reference.

**Clinical Instruction and Its Integration in the Curriculum.** By Deborah MacLurg Jensen, R. N., Instructor in Nursing Education and Sociology, University of Missouri. Third Edition. Pp. 542. Cloth. Price, \$5.75. St. Louis: C. V. Mosby Company, 1952.

This is a well outlined text book on nursing education. The author succeeds in combining theory and practice, emphasizing the value of clinical instruction. An attempt is made to prepare students to use all of their knowledge and skill in solving the problems facing them as they care for patients in institutions or in homes.

The book is divided into six sections, consisting of twenty-three chapters. The principles of planning, learning, teaching, and guidance are carefully outlined. Faculty organization and preparation is discussed. The last section (VI) outlines in detail integrated programs of clinical instruction in medical, surgical, pediatric, obstetric, and psychiatric nursing. An annotated bibliography is given at the end of each section.

The appendix gives illustrations of records for student nurses and sources for teaching aid. A subject index adds to the usefulness of the book.

Nursing schools and student and graduate nurses will find this a very valuable book.

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**Ward Administration.** By Deborah MacLurg Jensen, R. N., M. A., Instructor in Nursing Education and Sociology, University of Missouri. Illustrated. Pp. 335. Cloth. Price, \$4.00. St. Louis: C. V. Mosby Company, 1952.

This book deals principally with the administrative aspects of the head nurse in a general hospital, small or large. The modern qualifications and functions of the head nurse are well outlined. The material is well written and excellently organized. The book is divided into six sections which embody twenty-two chapters. The author outlines thoroughly and in detail the fundamental principles of administration, supervision, and teaching.

The appendix gives a sample ward manual or administrative guide, in which instructions are written governing all the ward activities and personnel.

An annotated bibliography is given at the end of each section of the book.

Nursing schools and nurses looking forward to advancement in hospital ward administration will find this book invaluable.

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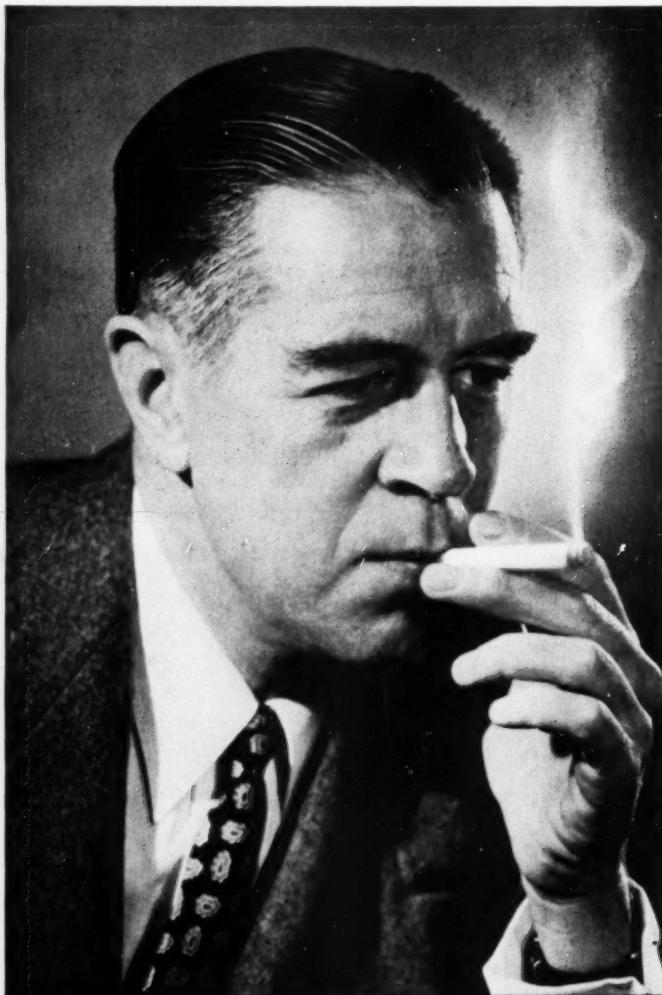


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2. Schwartzman, J.; Henderson, A. T., and King, W. E.: Hyaluronidase in Fluid Administration: A Preliminary Report, *J. Pediat.* 33:267 (Sept.) 1948.





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"Mother's asleep now, son," Dad told him. "She'll be asleep a long, long time. It's kind of like going away. We'll have to learn to get along without her, Johnnie."

## To a statistic named Johnnie

Who's Johnnie? Just one of the 175,000 children under eighteen here in the United States who have lost a mother to cancer.

Statistics are a little too big for a boy this small to understand. Even the hopeful ones about cancer—and there are more every year.

**More and more today—  
cancer can be cured**

*Patients are being cured who could not have been saved—even five years ago. In 1952, some 70,000 with cancer were saved.*

*And this number could have been doubled, if treatment in all the cases had been begun in time.*

Your contributions to the American Cancer Society helped make such hopeful statistics possible. And they can make the story even brighter tomorrow.

Not for Johnnie, to be sure.

But for all the other children—they might be yours—who still have their mothers and fathers. If only one tenth of the millions of people

like you who have such good intentions would actually take the time to send us their contributions! And would do it now—instead of turning the page . . .

**AMERICAN CANCER SOCIETY**

Gentlemen:

Please send me free literature about cancer. Enclosed is my contribution of \$\_\_\_\_\_ to the cancer crusade.

Name \_\_\_\_\_

Address \_\_\_\_\_

City \_\_\_\_\_ State \_\_\_\_\_

Simply address the envelope:  
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**CANCER STRIKES ONE IN FIVE**

**Strike back—give to the American Cancer Society**

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Operating Room in Hospital .....	10.00	20.00	30.00	40.00
Anesthetic in Hospital .....	10.00	20.00	30.00	40.00
X-Ray in Hospital .....	10.00	20.00	30.00	40.00
Medicines in Hospital .....	10.00	20.00	30.00	40.00
Ambulance to or from Hospital .....	10.00	20.00	30.00	40.00

**COSTS (Quarterly)**

Adult .....	2.50	5.00	7.50	10.00
Child to age 19 .....	1.50	3.00	4.50	6.00
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1. Frost, L. H., and Jackson, R. L.: J. Pediat. 39: 585-592, 1951.

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